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(19) (CA) **CANADIAN PATENT** (12)

(54) Microemulsions

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Canada

The present invention relates to aqueous microemulsions of agrochemical active compounds and/or active compounds for combating pests in the domestic and hygiene sectors. The invention also relates to a process for the preparation of these microemulsions and to their use.

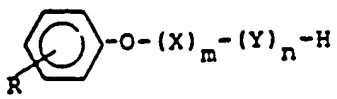
Oil-in-water emulsions of numerous agrochemical active compounds of low solubility in water are already known; in addition to the active compounds, these emulsions also contain, in each case, either a surface-active substance and a thickener or else a relatively large quantity of surface-active substances (compare DE-A (German Published Specification) 3,009,944, DE-A (German Published Specification) 3,011,611 and JP-A (Japanese Published Specification) 122,628-77). This addition of thickeners or of large quantities of surfactant is associated with additional expense and thus constitutes a serious disadvantage of the known oil-in-water emulsions. In addition to this, the preparation which has hitherto been described of emulsions of this type is not generally applicable. This is because, essentially, it is possible to emulsify by this process only those active compounds of low solubility in water which are liquid at room temperature or at least have a very low melting point. It is also disadvantageous that the known oil-in-water emulsions are frequently not adequately stable under cold conditions and that, in some cases, forced emulsification using homogenisers is required.

Aqueous microemulsions which contain

- 0.1 to 80% by weight of at least one agrochemical active compound of low solubility in water and/or one active compound for combating pests in the household and hygiene sectors,

1 to 20% by weight of a mixture of emulsifiers consisting of

a) at least one alkylaryl polyglycol ether of the formula



(I)

in which

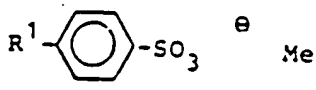
R represents alkyl having 8 to 20 carbon atoms,

X and Y each represent a $-CH_2-CH_2-O-$, $-CH_2-\underset{CH_3}{CH}-O-$ or $-\underset{CH_3}{CH}-CH_2-O-$ group, but X and Y do not simultaneously represent an oxyethylene or oxypropylene unit,

m represents numbers from 10 to 45 and

n represents numbers from 10 to 45, and

t least one alkylarylsulphonic acid salt of the ormula

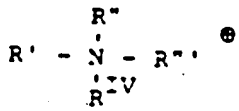


(II)

n which

R^1 represents alkyl having 8 to 35 carbon atoms and

$Me^{\oplus}$ represents an alkali metal cation, an equivalent of an alkaline earth metal cation or a cation of the formula

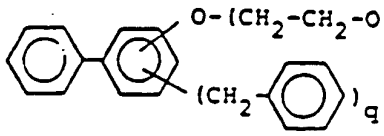


herein

R', R", R"' and R^{IV} independently of one

another represent hydrogen, alkyl having 1 to 4 carbon atoms or hydroxyalkyl having 1 to 4 carbon atoms, or

b) at least one alkylaryl polyglycol ether of the formula



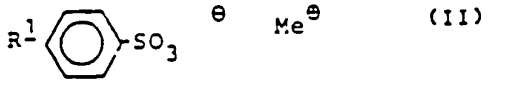
(III)

in which

p represents numbers from 5 to 20 and

q represents numbers from 1 to 3, and

at least one alkylarylsulphonic acid salt of the formula



(II)

in which

R^1 and $Me^{\oplus}$ have the meaning indicated above,

- and also water and
- if appropriate, 1 to 30% by weight of at least one organic solvent of low miscibility with water and/or of a solubiliser and also,
- if appropriate, 0.1 to 15% by weight of additives,

the sum of the components being in each case 100% by weight, have been found.

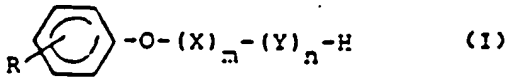
It has also been found that the microemulsions according to the invention can be prepared by adding, while stirring, to water optionally containing additives, a homogeneous mixture consisting of

- at least one agrochemical active compound of low solubility in water and/or one active compound for combating pests in the household and hygiene

sectors,

- a mixture of emulsifiers consisting of

a) at least one alkylaryl polyglycol ether of the formula

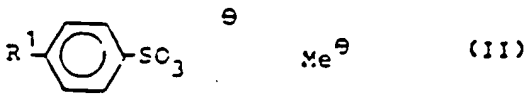


(I)

in which

R, X, Y, m and n have the meaning indicated above, and

at least one alkylarylsulphonic acid salt of the formula

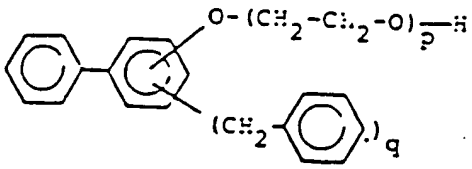


(II)

in which

R^1 and $Me^{\oplus}$ have the meaning indicated above, or

b) at least one alkylaryl polyglycol ether of the formula

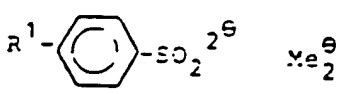


(III)

in which

p and q have the meaning indicated above, and

at least one alkylarylsulphonic acid salt of the formula



(II)

in which

R^1 and $Me^{\oplus}$ have the meaning indicated above,

- if appropriate, at least one organic solvent of low miscibility with water and/or a solubiliser, and also,
- if appropriate, additives.

Finally, it has been found that - depending on the active compounds they contain - the microemulsions according to the invention can be used for various purposes in agriculture or horticulture, or in the household and hygiene sectors.

It must be described as extremely surprising that the microemulsions according to the invention are stable, since it would have been expected on the basis of the known state of the art that emulsions of this type, which contain no thickeners and also only a small proportion of surfactant, would not be stable for a prolonged period. Thus it is apparent from DE-A (German Published Specification) 3,009,944 and DE-A (German Published Specification) 3,011,611 that the oil-in-water emulsions described in those texts necessarily contain a thickener as a stabiliser. The emulsions disclosed in JP-A (Japanese Published Specification) 122,628-77 have a very high proportion of surfactant in relation to the quantity of active compound. The excellent stability of the microemulsions according to the invention could not, therefore, have been foreseen.

The microemulsions according to the invention are distinguished by a number of advantages. Thus the expensive addition of thickeners or large quantities of emulsifiers is not necessary in their preparation. Furthermore, these emulsions contain either only an extremely small quantity of organic solvents or none at all. Therefore, they are incombustible and free, or at least virtually free, from odour troubles caused by organic solvents, and have a lower toxicity or phytotoxicity than corresponding

formulations containing organic solvents in the concentrations otherwise customary. In addition, the microemulsions according to the invention are stable under the conditions which prevail in practice. When stored for long periods, these emulsions remain unchanged both at temperatures of 50°C and at low temperatures. Finally, the microemulsions according to the invention can be prepared in a simple manner. Forced emulsification using homogenisers is not necessary. In addition, a very considerable advantage consists in the fact that active compounds of low solubility in water which are solid or liquid at room temperature can be emulsified with equal ease. Furthermore, the microemulsions according to the invention have a relatively low viscosity, so that accurate metering presents no difficulties. Finally, the microemulsions according to the invention are completely transparent preparations which can be diluted without problems in any desired ratio with water before use, stable, sprayable formulations being thus formed.

The microemulsions according to the invention contain at least one agrochemical active compound of low solubility in water and/or one active compound for combating pests in the household and hygiene sectors. These active compounds are present in the liquid state in the oil phase.

Suitable active compounds are substances which are liquid at room temperature, as well as those which are solid at room temperature. The only requirement for liquid active compounds is that they should be sparingly soluble in water. Compounds of this type are to be understood here as meaning substances which are soluble to the extent of not more than 0.5% by weight in water at 20°C. Solid active compounds must, however, additionally be adequately soluble in an organic solvent of low miscibility with water and/or in a solubiliser.

Agrochemical substances are to be understood in

the present case as meaning any active compounds which can customarily be used in plant protection. These include, for example, insecticides, acaricides, nematocides, fungicides, herbicides, growth regulators and fertilisers. The following may be mentioned as individual examples of active compounds of this type:

O,O-diethyl O-(4-nitrophenyl) thionophosphate,
O,O-dimethyl O-(4-nitrophenyl) thionophosphate,
O-(ethyl) O-(4-methylthiophenyl) S-propyl dithiophosphate,
(O,O-diethylthionophosphoryl)-α-oximinophenylacetonitrile,
2-isopropoxyphenyl N-methylcarbamate,
3-methylthio-4-amino-6-tert.-butyl-1,2,4-triazin-5-one,
3-methylthio-4-isobutylideneamino-6-tert.-butyl-1,2,4-triazin-5-one,
2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine,
2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate,
3,5-dimethyl-4-methylthiophenyl N-methylcarbamate,
O,O-diethyl O-(3-chloro-4-methyl-7-coumarinyl) thiophosphate,
6,7,8,9,10,10-hexachloro-1,5,5A,6,9,9A-hexahydro-6,9-methane-2,3,4-benzodioxathiepin-3-oxide,
1,4,5,6,7,8,8-heptachloro-4,7-endomethylene-3A,4,7,7A-tetrahydroindene,
2-(2-furyl)-benzimidazole,
5-amino-1-bis-(dimethylamido)-phosphoryl-3-phenyl-1,2,4-triazole,
4-hydroxy-3-(1,2,3,4-tetrahydro-1-naphthyl)-coumarin,
S-[1,2-bis-(ethoxycarbonyl)-ethyl] O,O-dimethyl dithiophosphate,
O,O-dimethyl O-(4-methylmercapto-3-methylphenyl) thionophosphate,
O-ethyl-O-(2-isopropoxycarbonylphenyl)-N-isopropylthionophosphoric acid ester-amide,
1-(4-chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)-2-butanone,
(S)-α-cyano-3-phenoxybenzyl (1R)-cis-3-(2,2-dibromovinyl)-

2,2-dimethylcyclopropanecarboxylate and α-cyano-3-phenoxy-4-fluorobenzyl 2,2-dimethyl-3-(β,β-dichlorovinyl)-cyclopropanecarboxylate.

Active compounds for combating pests in the domestic and hygiene sectors are to be understood, in the present case, as meaning any customary active compounds of low solubility in water which are suitable for indications of this type. The following may be mentioned as individual examples of active compounds of this type:

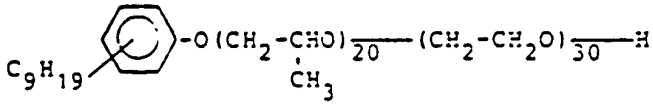
2-isopropoxyphenyl N-methylcarbamate,
0,0-diethyl 0-(4-nitrophenyl) thionophosphate,
0,0-dimethyl 0-(4-nitrophenyl) thionophosphate,
s-[1,2-bis-(ethoxycarbonyl)-ethyl] 0,0-dimethyl dithiophosphate,
0,0-dimethyl 0-(3-methyl-4-nitrophenyl) thionophosphate,
0,0-dimethyl 0-(4-methylmercapto-3-methylphenyl) thionophosphate,
γ-hexachlorocyclohexane and
(cyclohex-1-ene-1,2-dicarboximidomethyl) 2,2-dimethyl-3-(2-methylpropenyl)-cyclopropanecarboxylate.

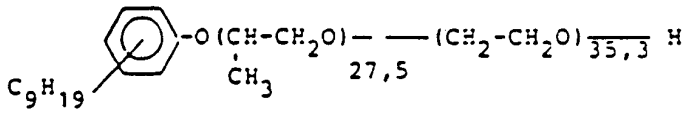
The emulsifier mixtures present in the microemulsions according to the invention consist of either at least one alkylaryl polyglycol ether of the formula (I) and at least one alkylarylsulphonic acid salt of the formula (II), or at least one alkylaryl polyglycol ether of the formula (III) and at least one alkylarylsulphonic acid salt of the formula (II).

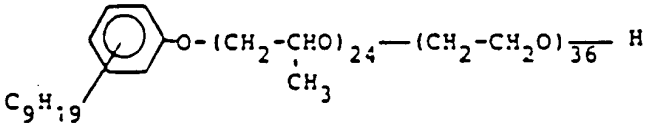
The alkylaryl polyglycol ethers of the formula (I) are defined in a general manner by the formula

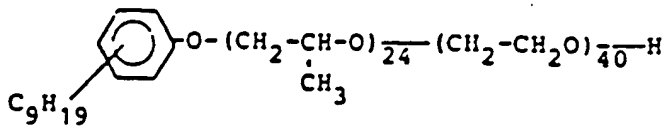
indicated. In this formula, R preferably represents alkyl having 10 to 18 carbon atoms. X and Y each represent a $-CH_2-CH_2-O-$, $-CH_2-\underset{CH_3}{CH}-O-$ or $-\underset{CH_3}{CH}-CH_2-O-$ group, but X and Y do not simultaneously represent an oxyethylene or oxypropylene unit. The index m preferably represents numbers from 12 to 30 and the index n preferably represents numbers from 12 to 40. The numbers for the indices m and n represent average values.

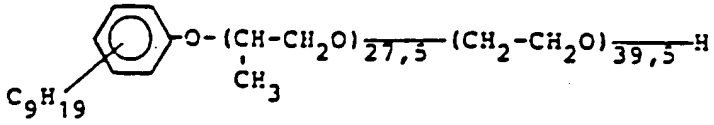
The emulsifiers of this type which are used in practice are generally mixtures composed of several compounds of the formula (I). In particular, they are mixtures composed of substances of the formula (I), differing in the number of oxyethylene and/or oxypropylene units. Calculation thus also yields fractional numbers as average values for the indices m and n. Substances for which the following average compositions result may be mentioned as examples:

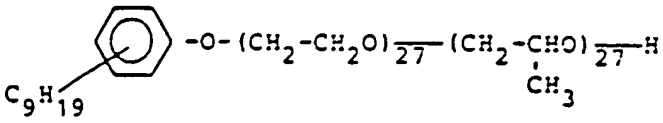






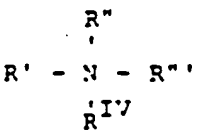






The alkylaryl polyglycol ethers of the formula (I) are known.

The alkylarylsulphonic acid salts present in the microemulsions according to the invention are defined in a general manner by the formula (II). In this formula, R^1 preferably represents straight-chain or branched alkyl having 9 to 30 carbon atoms. $Me^{\oplus}$ preferably represents a sodium cation, one equivalent of a calcium cation or a cation of the formula



wherein

R', R'', R''' and R^{IV} independently of one another preferably represent hydrogen, alkyl having 1 or 2 carbon atoms or hydroxyalkyl having 1 to 2 carbon atoms.

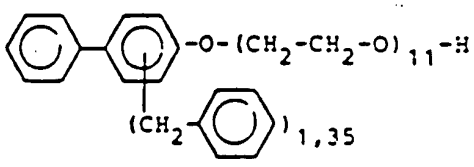
The following may be mentioned as individual examples of alkylarylsulphonic acid salts of the formula (II):

sodium 4-(n-nonyl)-phenylsulphonate,
calcium 4-(n-dodecyl)-phenylsulphonate,
sodium 4-(tetrapropylene)-phenylsulphonate,
calcium 4-(n-nonyl)-phenylsulphonate,
ammonium 4-(i-dodecyl)-phenylsulphonate and
(2-hydroxyethyl)-ammonium 4-(n-dodecyl)-phenylsulphonate.

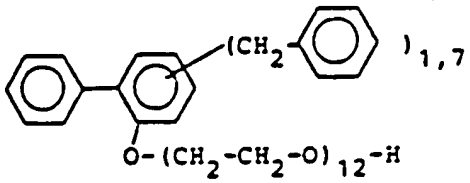
The alkylarylsulphonic acid salts of the formula (II) are known. They are generally employed in the form of 50-75% strength solutions in organic solvents, for example n-butanol, i-butanol or benzyl alcohol, but can, in principle, also be used without a solvent.

The alkylaryl polyglycol ethers of the formula (III) are defined in a general manner by the formula indicated. In this formula, the index p preferably represents numbers from 8 to 18, and the index q preferably represents numbers from 1 to 2. The numbers for the indices p and q represent average values.

The emulsifiers of this type which are used in practice are generally mixtures composed of several compounds of the formula (III). In particular they are mixtures composed of substances of the formula (III), differing in the number of oxyethylene units and/or in the degree of substitution on the phenyl radical. Calculation can thus also yield fractional numbers as average values for the indices p and q. Substances for which the following average compositions result may be mentioned as examples:



and



The alkylaryl polyglycol ethers of the formula (III) are also known.

Any customary organic solvents of low miscibility with water are suitable as the organic solvents which can, if appropriate, be present in the microemulsions according to the invention. Solvents which may be mentioned preferentially are aromatic hydrocarbons, such as xylene, toluene and dimethylnaphthalene, and also chlorinated aromatic hydrocarbons, such as chlorobenzenes, and also aliphatic hydrocarbons, such ligroin and petroleum ether, additionally halogenated aliphatic hydrocarbons, such as methylene chloride and chloroform, additionally cycloaliphatic hydrocarbons, such as cyclohexane, and also alcohols and ketones, such as n-butanol, n-hexanol, isohexanol, n-octanol, cyclohexanol, benzyl alcohol, di-n-butyl ketone and isophorone, and also ethers and esters, such as glycol monomethyl ether and glycol monomethyl ether-acetate, and, furthermore, also triethyl phosphate.

Any customary solubilisers are suitable as the solubilisers which can be present in the microemulsions according to the invention. Solubilisers which can be used preferentially are alkylphenols or cresols which have been subjected to a condensation reaction with, per mol, 1 to 8 mols of ethylene oxide. p-Cresol which has been subjected to a condensation reaction with, per mol, 1 to 8 mols of ethylene oxide should be mentioned specially in this connection.

Suitable additives which can, if appropriate, be present in the microemulsions according to the invention are preservatives, dyestuffs, cold stabilisers and

synergists.

2-Hydroxybiphenyl and sorbic acid may be mentioned as examples of preservatives. Azo dyestuffs and phthalocyanine dyestuffs may be mentioned as examples of dyestuffs. Urea, sugars and salts, such as ammonium sulphate and sodium oleate, may be mentioned as examples of cold stabilisers. 3,4-Methylenedioxy-6-propylbenzyl-n-butyldiethylene glycol ether (piperonyl butoxide) may be mentioned as an example of a synergist.

The percentage proportions of the components present in the microemulsions according to the invention can be varied within specific ranges. In general, the proportion of active compound or active compounds is between 0.1 and 80% by weight, preferably between 5 and 80% by weight. The proportion of emulsifier mixture is, in general, 1 to 20% by weight, preferably 3 to 16% by weight, and the ratio of the emulsifiers to one another can also be varied within a specific range. In general, there is 0.2 to 1.2, preferably 0.4 to 1, part of emulsifier of the formula (II) to 1 part of emulsifier of the formula (I). Furthermore, there is, in general, 0.1 to 1.2 parts, preferably 0.2 to 1.0 part, of emulsifier of the formula (II) to 1 part of emulsifier of the formula (III).

Organic solvents of low miscibility with water and/or solubilisers can be present in proportions of 1 to 30% by weight, preferably 5 to 20% by weight. Additives can be present in proportions of 0.05 to 15% by weight, preferably 0.1 to 10% by weight. The percentage proportion of water in the microemulsions according to the invention is in each case the difference between 100% by weight and the total of the percentage proportions of the other components.

The ratio of active compound(s), on the one hand, optionally mixed with organic solvents and/or solubilisers, to the emusifier mixture on the other hand can be varied within a specific range in the microemulsions according to

the invention. In general, there are 1 to 15 parts by weight, preferably 2 to 10 parts by weight, of active compound(s), if appropriate mixed with organic solvents and/or solubilisers, to 1 part of emulsifier mixture.

In preparing the microemulsions according to the invention it can be preferable to use all the components which have already been mentioned preferentially in connection with the description of the microemulsions according to the invention.

If an active compound which is in the liquid state at temperatures up to 40°C is used in the process according to the invention, it is generally unnecessary to add an organic solvent and/or a solubiliser of low miscibility with water.

If, on the other hand, an active compound which is in the solid state at temperatures up to 40°C is used in the process according to the invention, it is necessary to dissolve the active compound concerned in an organic solvent of low miscibility with water and/or a solubiliser before emulsification. The quantity of organic solvent and/or solubiliser in this case is such that it is exactly sufficient to dissolve the solid substance.

The reaction temperatures in the process according to the invention can be varied within a fairly wide range. In general, the process is carried out at temperatures between 10°C and 80°C, preferably between 20°C and 60°C.

The method generally followed in carrying out the process according to the invention is first to prepare a homogeneous solution consisting of one or more active compounds, an emulsifier mixture, if appropriate an organic solvent of low miscibility with water and/or a solubiliser and, if appropriate, additives, and then to add this mixture, while stirring, to water, if appropriate containing additives. In doing so, the quantities of the components are selected in such a way that the components in the resulting microemulsion are present in the concentration

desired in the particular case. The sequence in which the components of the organic phase are combined can be varied. The addition of the organic phase to the aqueous phase is advantageously effected slowly, while stirring uniformly with customary stirring equipment. In the course of this, a finely disperse, transparent microemulsion which can no longer be distinguished optically from a solution, is formed.

The microemulsions according to the invention can be applied either in the form in which they have been prepared or after prior dilution. The quantity applied depends on the concentration of the active compounds in the microemulsion and on the particular indication.

The use of the microemulsions according to the invention is effected by the customary methods, that is to say, for example, by spraying, sprinkling or pouring.

The preparation of the microemulsions according to the invention can be seen from the following examples.

Preparation Examples

Example 1

8 g of an emulsifier mixture consisting of

- 6 parts by weight of a nonylphenol polyglycol ether which has an average of 27 oxyethylene and 27 oxypropylene units per molecule,

and

- 4 parts by weight of calcium 4-(n-dodecyl)-phenyl-sulphonate (dissolved in n-butanol),

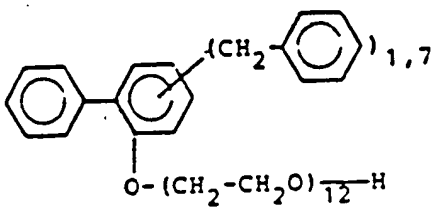
is added, at temperatures between 20°C and 40°C and while stirring, to 70 g of the insecticidal active compound 0,0-dimethyl O-(4-methylmercapto-3-methylphenyl) thionophosphate. The homogeneous solution thus formed is poured, in the course of 2 minutes and while stirring vigorously, into 22 g of deionised water. When the addition is complete, stirring is continued for a further 5 minutes. A transparent microemulsion is formed, which exhibits no physical or chemical changes even after storage at elevated

temperature for several weeks.

Example 2

14 g of an emulsifier mixture consisting of

- 10 parts by weight of an alkylaryl polyglycol ether, the average composition of which can be seen from the following formula



and

- 4 parts by weight of calcium 4-(n-dodecyl)-phenylsulphonate (dissolved in n-butanol),

are added, at temperatures between 20 and 40°C and while stirring, to 50 g of 0,0-dimethyl O-(4-methylmercapto-3-methylphenyl) thionophosphate. The homogeneous solution thus formed is added, in the course of 2 minutes and while stirring vigorously, to 36 g of deionised water. When the addition is complete, stirring is continued for a further 5 minutes. A transparent microemulsion is formed, which exhibits no physical or chemical changes even after storage at elevated temperature for several weeks.

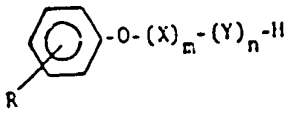
THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. An aqueous microemulsion comprising:

A. 0.1 to 80% by weight of at least one agrochemically active compound of low solubility in water and/or one active compound for combating pests in the household and hygiene sectors, and

B. 1 to 20% by weight of a mixture of emulsifiers selected from

a) a mixture of at least one alkylaryl polyglycol ether of the formula



(I)

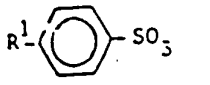
in which

R represents alkyl having 8 to 20 carbon atoms,

X and Y each represent a $-CH_2-CH_2-O-$, $-CH_2-\underset{CH_3}{CH}-O$ or $-\underset{CH_3}{CH}-CH_2-O-$ group, but X and Y do not simultaneously represent an oxyethylene or oxypropylene unit,

m represents numbers from 10 to 45 and

n represents numbers from 10 to 45, with at least one alkylarylsulphonic acid salt of the formula



(II)

in which

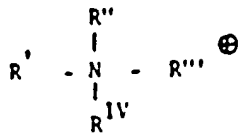
R^1 represents alkyl having 8 to 35 carbon atoms and

$Me^{\oplus}$ represents an alkali metal cation, an

B

equivalent of an alkaline earth metal cation

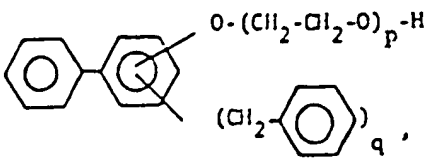
or a cation of the formula



wherein

R', R'', R''' and R^{IV} independently of one another represent hydrogen, alkyl having 1 to 4 carbon atoms or hydroxyalkyl having 1 to 4 carbon atoms, or

b) a mixture of at least one alkylaryl polyglycol ether of the formula



(III)

in which

p represents numbers from 5 to 20 and

q represents numbers from 1 to 3, with at least one alkylarylsulphonic acid salt of formula (II) defined above, the sum of the recited components and the water being in each case 100% by weight.

2. An aqueous microemulsion according to Claim 1, wherein the microemulsion contains 1 to 30% by weight of at least one organic solvent of low miscribility with water and/or a solubilizer.

3. An aqueous microemulsion according to Claim 1, wherein the microemulsion contains 0.05 to 15% by weight of an additive.

4. A microemulsion according to Claim 2, wherein said organic solvent is an aromatic hydrocarbon, chlorinated aromatic hydrocarbon, aliphatic hydrocarbon, chlorinated aliphatic hydrocarbon, alcohol, ketone, ether, ester or trialkyl phosphate.

5. A microemulsion according to Claim 4, wherein said organic solvent is selected from the group consisting xylene, toluene, dimethylnaphthalene, ligroin, petroleum ether, methylene chloride, chloroform, cyclohexane, n-butanol, n-hexanol, isohexanol, n-octanol, cyclohexanol, benzyl alcohol, di-n-butyl ketone =, isophorone, glycol monomethyl ether, glycol monomethyl ether-acetate and triethyl phosphate.

6. A microemulsion according to Claim 3, containing as an additive, a preservative, dyestuff, cold stabilizer or synergist.

7. A microemulsion according to Claim 1, wherein component A is an agrochemically active compound.

8. A microemulsion according to Claim 7, wherein said agrochemically active compound is an insectide, acaricide, nematocide, fungicide, herbicide, plant growth regulator or fertilizer.

9. A microemulsion according to Claim 8, wherein said agrochemically active compound is a compound selected from the group consisting of:

O,O-diethyl O-(4-nitrophenyl) thionophosphate,

O,O-dimethyl O-(4-nitrophenyl) thionophosphate,

O-(ethyl) O-(4-methylthiophenyl) S-propyl dithiophosphate,

(O,O-diethylthionophosphoryl)-α-oximinophenylacetonitrile,

2-isopropoxyphenyl N-methylcarbamate,

3-methylthio-4-amino-6-tert.-butyl-1,2,4-triazin-5-one,

3-methylthio-4-isobutylideneamino-6-tert.-butyl-1,2,4-triazin-5-one,

2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine,

2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate,

3,5-dimethyl-4-methylthiophenyl N-methylcarbamate,

O,O-diethyl O-(3-chloro-4-methyl-7-coumarinyl) thiophosphate,

6,7,8,9,10,10-hexachloro-1,5,5A,6,9,9A-hexahydro-6,9-methane-2,3,4-benzodioxathiepin-3-oxide,

1,4,5,6,7,8,8-heptachloro-4,7-endomethylene-3A,4,7,7A-tetrahydroindene,

2-(2-furyl)-benzimidazole,

5-amino-1-bis-(dimethylamido)-phosphoryl-3-phenyl-1,2,4-triazole,

4-hydroxy-3-(1,2,3,4-tetrahydro-1-naphthyl)-coumarin,

S-[1,2-bis-(ethoxycarbonyl)-ethyl] O,O-dimethyl dithiophosphate,

O,O-dimethyl O-(4-methylmercapto-3-methylphenyl) thionophosphate,

O-ethyl-O-(2-isopropoxycarbonylphenyl)-N-isopropylthiono-

LIQUID ACTIVE INGREDIENT CONCENTRATES FOR PREPARATION OF MICROEMULSIONS

The invention concerns new active ingredient formulations as claimed in claims 1–8, and their application for the production of so-called microemulsions, in which the lipid phase is present with a fineness of 10–200 nm.

Many active effective substances, e.g. pharmaceutical active substances or pesticides, are poorly soluble or insoluble in water, making it impossible to produce homogeneous liquid forms of application.

DE-OS No. 30 42 365 describes liquid, single-phase multi-substance systems containing lecithin, which systems contain active ingredients that are poorly soluble or insoluble in amphiphilic phospholipids. The system contains viscosity regulators in the form of glycerine esters of fatty acid and/or acylated and/or methoxylated derivatives of these glycerine esters or polyether glycols. The systems are shiny, oily liquids.

These liquids cannot, however, be diluted with water to form stable, finely divided emulsions—so-called microemulsions; instead the result is separations, precipitations, and non-homogeneous systems.

The objective of the invention is to create homogeneous, liquid, active ingredient formulations with active ingredients that are insoluble or poorly soluble in water, formulations which can be diluted with any quantity of water and thus, as application preparations, form homogeneous, transparent emulsions.

This objective is achieved by the liquid active ingredient formulations described in the patent claims and by their application in the production of microemulsions.

Surprisingly, it was found that homogeneous, liquid, transparent active ingredient concentrates can be produced with active ingredients that are insoluble or poorly soluble in water, concentrates which can be mixed with water in any ratio.

The liquid active ingredient formulation under the invention is a lipophilic liquid containing phospholipids or phospholipid mixtures, a co-emulsifier, a lipophilic carrier liquid, and the active ingredient. Water can be added to this lipophilic active ingredient concentrate in any quantity without its transparency being lost. This creates application formulations which contain the active ingredient(s) in homogeneous form in a lipid phase; the active ingredients are present in this preparation, which is ready for application, in the form of O/W microemulsions, with a particle or micro-droplet size of 10–200 nm. These transparent emulsions, or, as understood in this invention, application preparations, which result from the dilution of the lipophilic concentrates with water, can involve micellar dispersions as well as microemulsions, in which the droplet size in the dispersion phase has a colloidal magnitutde (Leon M. Price, Microemulsions, Academic Press, Inc.).

The phospholipids employed in the invention concentrate formulations can be mixtures of phosphatidyl choline, phosphatidyl ethanol amine, N-acylphosphatidyl ethanol amine, phosphatidic acid, or phosphatidyl inositol, particularly phospholipids with a phosphatidyl choline content of 30–95%.

The co-emulsifier can be glycerin in which the 1 or 2 OH groups have been esterized by means of saturated fatty acids with hydrocarbon chains of 8–16, preferably 8–10 C atoms, and the third or remaining OH group of the glycerin body is etherized with polyethylene glycol, specifically with 6–30, preferably 6–15, ethylene oxide units. The HLB values of these co-emulsifiers (following Griffin) are between 12 and 18, preferably between 15 and 17.

Examples of these co-emulsifiers are a water-soluble partial glyceride mixture of natural, saturated vegetable oil acids of moderate chain length, in the form of a viscous oil, re-esterized polyethoxylized caprylic acid/capric acid glyceride (PEG-6-caprylic acid/capric acid glyceride, polyoxyethylene-glycerin monolaurate with HLB 15.7, polyoxyethylene-glycerin ricinocteate with HLB 14).

Suitable carrier liquids are glycerides compatible with phospholipids, to which suitable low esters have been added, particularly fatty acid esters, for example, acetic acid ethyl ester, isopropyl myristate or isopropyl palmitate.

To improve compatibility with the phospholipids, organic solvents can be added, which must be miscible with water at any ratio, for example, lower alcohols with C_{1-4} carbon atoms, dimethyl formamide, dimethyl amine or 2-dimethyl-4-hydroxy methyl-1,3 dioxalane.

The usual auxiliary agents, such as antioxydants, complex formers, or preservatives, can also be added.

Essential for the formation of microemulsions from the concentrates is the molar ratio of the phospholipid to the co-emulsifier. This ratio can be from 1:1 to 1:4, preferably 1:1 to 1:2. A ratio of 1:2 is particularly recommended. The quantity of carrier liquid also influences the formation of the microemulsion.

The invention active ingredient concentrates from which the application preparations are produced through the addition of certain quantities of water have the following compositions:

5–50 wght.% phospholipids
5–80 wght.% co-emulsifier
10–60 wght.% carrier liquid
0.1–50 wght.% active ingredient
0.1–10 wght.% other additives and auxiliary agents

To produce the new active ingredient concentrates the phospholipid is dissolved under slight heat in the solvent or solvent mixture while being stirred. The co-emulsifier and other auxiliary agents are stirred into the homogeneous liquid. The active ingredient is then added and stirred under low heat up to a maximum of 60° C. and is stirred until the homogeneous phase is reached. A microemulsion forms from this homogeneous, predominantly lipophilic phase when the liquid is diluted with water, and represents the preparation ready for use.

The active ingredients can be pharmaceutical active substances insoluble in water or plant protectants with a herbicidal, fungicidal, insecticidal, acaricidal, nematocidal effect or with an effect regulating plant growth.

From the group of herbicides, e.g.:

N-phosphone methyl glycin (glyphosat),
3-(2-chloro-4-methyl-phenyl)-1,1-dimethyl urea (chlortoluron),
N-(4-methoxy-6-methyl-1,3,5-triazine-2-yl)-aminocarbonyl-2-chlorophenyl sulfonamide,
3-(4-isopropyl-phenyl)-1,1-dimethyl urea (isoproturon),
3-methyl-4-amino-6-phenyl-1,2,4-triazine-5(4H)-on (metamitron),
1,3-dimethyl-3-(2-benzthiazolyl)-urea (methabenzthiazuron),
2-chloro-4-ethylamino-6-isopropylamino-s-triazine (atrazine)
3-(3,4-dichlorophenyl)-1-methoxy-1-urea (linuron),